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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09.576.057	05/23/2000	Joseph Chappell	07678-011004	3528

21559 7590 08/29/2003

CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

EXAMINER

NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 08/29/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory ActionApplication No.
09/576,057Applicant(s)
Chappell et al.Examiner
Nashaat T. NashedArt Unit
1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED Jul 28, 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY (check only a) or b))

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
- b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see NOTE below);
- (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See attached.

3. ☐ Applicant's reply has overcome the following rejection(s): _____

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: None

Claim(s) objected to: None

Claim(s) rejected: 1-5

Claim(s) withdrawn from consideration: _____

8. The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

10. Other: _____

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER

Claims 1-5 are pending as they relate to tobacco-*Hyoscyamus* CH4 chimeric isoprenoid synthase.

The terminal disclaimer filed on July 28, 2003 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U. S. Patent 5,824,744 has been reviewed and is accepted. The terminal disclaimer has been recorded.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons set forth in the prior Office action, see paper number 9.

In response to the above objection, applicant traverse the compliance requirement on the ground that: (1) knowledge of nucleic and amino acid sequences aren't needed to carry out the type of manipulations that are described and claimed in the present application; and (2) the present application has the same specification as USSN 08/631,341 (USP 5,824,774) and 09/134,699 (USP 6,072,045).

Applicant arguments filed 7/28/03 have fully considered and they are found unpersuasive. First, the application describes an invention with reference to specific nucleic and amino acid sequences with specific references to amino acid residues in a specific amino acid sequences. While chimeric proteins has been made in the past by cutting specific nucleic acid sequences encoding protein domains using a specific restriction enzymes and joining the pieces together, the specific nucleic acid were determined to have the specific restriction sites from their nucleic acid sequences. In addition, the teaching of the specification appears to identify important amino acid residues in the exemplary sequences to guide one of ordinary skill in the art to identify the various domains in order to obtain a chimeric protein having some new activity(ies). Thus, without the nucleic and acid sequences one of ordinary skill in the art would not be able to carry out the claimed invention. The compliance with the sequence rule is mandatory for patent application containing nucleic/amino acid sequence. As for the issued patent, they are irrelevant to the prosecution of the instant application, and neither one of them is under consideration at this time. Applicants are reminded that an issued patent is presumed to be in compliance with all the requirements for a patent under 35 U. S. C. 282. If applicants would like either or both patents to be reconsidered, they may refile a request for reissue.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact

terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons set forth in the prior Office actions, see papers numbers 9 and 12.

In response to the above rejections, applicants traverse the rejection on the ground that the genes and the restriction sites of isoprenoid synthases are highly conserved, one of ordinary skill in the art does not have to know the structure of each and every isoprenoid synthase.

Applicant arguments filed 7/28/03 have been fully considered, and they are found unpersuasive. As indicated in the previous Office actions, papers numbers 9 and 12, the specification teaches several chimeric polypeptides from TEAS and HVS synthases. Applicants have identified these chimeric polypeptide by cutting and pasting nucleic acid fragments using restriction enzymes, see the previous Office action, paper number 12. Applicants have not provided any evidence to support their claim that restriction sites in genes encoding isoprenoid synthases are conserved among the vast majority of said genes. While it may be true that one ordinary skill in the art does not need to know the domain structure of two polypeptide to make a chimeric polypeptide, the function of the resulting polypeptide is highly unpredictable without the structural information. The claimed chimeric polypeptide can have any isoprenoid synthase activity and not a specific activity. The specification has failed to describe structure activity relationship which guide the ordinary skill in the art to construct a functional chimeric polypeptide having a specific catalytic activity(ies). Applicant should note the claims lack both function and structure limitation. Isoprenoid synthase is a non-specific function.

Claims 1-5 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to chimeric synthase produced by cutting and pasting the tobacco TEAS and *Hyoscyamus* HVS genes for the reasons set forth in the prior Office actions, papers numbers 9 and 12.

In response to the above rejections, applicant traverse the rejections on the ground that the genes and the restriction sites of isoprenoid synthases are highly conserved, one of ordinary skill in the art does not have to know the structure of each and every isoprenoid synthase. Also, they argue the U. S. P. T. O. has routinely issued patents for polypeptide and genes having altered activities.

Applicant arguments filed 7/28/03 have been fully considered, and they are found unpersuasive. As indicated in the previous Office actions, papers numbers 9 and 12, the specification teaches several chimeric polypeptides from TEAS and HVS synthases. Applicants have identified these chimeric polypeptide by cutting and pasting nucleic acid fragments using restriction enzymes, see the previous Office action, paper number 12. Applicants have not provided any evidence to support their claim that restriction sites in isoprenoid synthases are conserved among the vast majority of said genes. While it may be true that one ordinary skill in the art to know the domain structure of two polypeptide to make a chimeric polypeptide, the function of the resulting polypeptide is highly unpredictable without the structural information. The claimed chimeric polypeptide can have any isoprenoid synthase activity and not a specific activity. Thus, searching for a chimeric polypeptide having a specific catalytic activity(ies) would require undue experimentation.

Claims 1-5 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The phrase "comprising a first isoprenoid synthase polypeptide joined to a second, different isoprenoid synthase polypeptide" in claim 1 render the claim indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired for the reasons set forth in the prior Office action, paper number 9.
- (d) claims 2-5 are included in these rejection because they are dependent on rejected claims and do not cure its deficiencies.

Applicants argue that the proposed amendment to the claims overcome this rejection.

Applicants' arguments filed 7/28/03 have been fully considered but they are not deemed to be persuasive. The examiner disagrees with applicants argument. The new phrase "at least a portion of a firstat least a portion of a second" in claims 1-3 raises new indefiniteness issues. Thus, the new amended claims will not be entered to the record upon filing the appeal brief.

No claim is allowed.

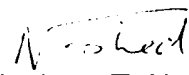
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Nashaat T. Nashed, Ph. D.
Primary Examiner